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THE TREATMENT DYNAMICS ASSESSMENT AMONG PATIENTS WITH CHRONIC VIRAL HEPATITIS B, INFECTED WITH HUMAN IMMUNODEFICIENCY VIRUS

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Abstract

Introduction: the article represents prospective study results of the treatment dynamics among patients with chronic viral hepatitis B, infected with human immunodeficiency virus. Particularly, the role of qHBsAg dynamics in the serum concerning CHB treatment effectiveness of CHB/HIV coinfecting patients as well as clinical and laboratory factors influencing on this marker.

The study purpose: To assess treatment dynamics of CHB/HIV coinfecting patients basing on quantitative HBsAg determination and other clinical and laboratory test applying.

Material and methods: 60 coinfecting patients were examined – the main group, 60 CHB mono-infected patients – comparison group to reach established study purpose. Diagnosis of HIV and chronic hepatitis B were verified. A clinical, laboratory, serological, molecular-genetic methods were used. Statistical processing of results was held with applying parametric and nonparametric methods for the data analysis.

Research results: There was a slight increase by 1.10 times in serum ALT in “a period of ≤ 6 months of antiviral therapy” with a subsequent decrease by 1.20-1.46 times in “a period of > 6 months of therapy”. There was a decrease in the serum qHBsAg of coinfecting patients in accordance with the duration of therapy by 1.56-21.10 times, and in case of the presence of "ALT flare" by 1.31-72.72 times. The greatest decrease in serum qHBsAg by 1.63-42.00 times during HAART was also observed in patients with an initial CD4 + count < 350 cells / μl . A serum qHBsAg was 11.24 times lower after > 12 months of therapy in the group of CHB/HIV coinfecting patients with $\Delta\text{CD4} + > 100$ cells / μl compared with the group of patients with $\Delta\text{CD4} + 0 - 100$ cells / μl .

Conclusions: A serum qHBsAg possibly to be decreased by 2 log₁₀ among CHB/HIV coinfecting patients after starting HAART with dual activity against HBV and HIV which includes nucleoside reverse transcriptase analogs (Tenofovir Disoproxil Fumarate (TDF) and lamivudine (3TC)). Defined main influencing factors on qHBsAg decreasing included: “ALT flare”, CD4+ count, $\Delta\text{CD4}+$ as a result of monofactorial analysis. It is necessary to conduct further multifactorial analysis to determine complex of factors which could influence on further HBsAg by 2 log₁₀ and HBsAg clearance.

Key words: CHB/HIV coinfection; quantitative determination of HBsAg (qHBsAg); HBV DNA; CD4+; $\Delta\text{CD4}+$; “ALT flare”; hardly active antiretroviral therapy (HAART).

Introduction: Almost 7.4% of HIV-infected patients have HBV infection around the world, which is one of the main causes of mortality in this category of patients [5].

Chronic hepatitis B remains a difficult problem for patients with HIV, as a result of common transmission ways, acceleration in the development of the liver cirrhosis and hepatocellular carcinoma in 25% - 40% of cases [10].

Implementation of the highly active antiretroviral therapy (HAART) with double antiviral activity drug applying against hepatitis B virus (HBV) and human immunodeficiency virus (HIV), namely, Tenofovir Disoproxil Fumarate (TDF), provides a way to reduce the viral load of CHB, stopping fibrotic changes in the liver and improving the quality of life of this group of patients [1].

However, the treatment effectiveness markers for CHB patients coinfecting with HIV infections still undeveloped. The role of qHBsAg dynamics in the serum concerning CHB treatment effectiveness as well as the quantitative HBsAg levels detection in the serum has not been established. Moreover, factors that can influence the dynamics of HBsAg levels in

coinfected patients such as: the paradoxical rise of ALT (“ALT flare”) in the beginning of the antiviral therapy start, the CD4+ count, etc. which remains not studied enough, thus justify the chosen topic actuality.

Purpose: To assess treatment dynamics of CHB/HIV coinfecting patients basing on quantitative HBsAg determination and other clinical and laboratory test applying.

Material and methods: There was planned and performed prospective cohort study. 60 coinfecting patients were examined – the main group, 60 CHB monoinfected patients – comparison group to reach established study purpose. All patients were under medical observation in Vinnytsia regional clinical AIDS Center and Vinnytsia regional clinical hospital # 1, Vinnytsia, Ukraine.

The average age of the patients included into the main group was 34.57 ± 7.99 years, men prevailed in the gender structure 40 (66.67%), and women’s fraction was 20 (33.35%) people. The average age of the patients included into the comparison group was $34,60 \pm 9,99$, men among them 36 (60,00 %), women - 24 (40,00 %).

Diagnosis of HIV and chronic hepatitis B were verified.

There were used the next laboratory methods:

- ALT and AST levels determinations with using the automatic biochemical analyser “Vitalab Flexor” (IU/ml);

- quantitative HBsAg determination with the help of immunochemiluminiscent test «HBsAg Architect Kit (6C36)» created by «Abbott Laboratories» with the using of automatic analyser «Architect» (IU/ml);

- HBV DNA with the using of real time PCR analyser “m2000rt Instrument System” created by Abbott Molecular Inc., USA;

- biochemical index APRI for the fibrosis level determination: $APRI = (AST/(ULN AST)) * 100 / \text{platelets (109/l)}$.

HIV diagnosis verification was performed with the using anti-HIV with ELISA method “Sanrise RC, Switzerland” accordingly with Ukrainian legislation.

CD4+ count with the method of citofluorometry was performed using “EPICS-XL” (cells/ml).

All coinfecting patients who were included into main group after diagnosis verification and basic examination performing were prescribed HAART with double activity against HIV and CHB with the obligatory prescription of nucleoside analogs of reverse transcriptase (NRTI’s – TDF/3TC or TDF/FTC) and third component as well. Antiviral therapy with NRTI’s for monoinfected patients as well was prescribed in form of TDF.

Statistical processing of results was held in the system of statistical data analysis “IBM SPSS Statistics, version 12” (license № 9593869, belongs to infectious diseases department of National Pirogov Memorial Medical University, Vinnytsya, Ukraine) with applying parametric and nonparametric methods for the data analysis.

A correlation with the “Spearman rank correlation coefficient” has been performed to define relations between more than two parameters before treatment starting. Odds ratio (OR) with the confidential interval (CI) in case of data comparison before treatment have been applied as well. It has been calculated “mean” (M) and standard deviation (σ) and parametric tests in case of “normally distributed data”. It has been calculated “median” (Me) and interquartile range (Q1 – Q3) and non-parametric tests in case of “not normally distributed data”.

Results: Correlation analysis has been carried out in order to assess the relationships between variables. There were received a different strength and direction correlations of qHBsAg with factors indicated in table 1.

A positive, strong correlation of qHBsAg in the blood serum with the HBV DNA level was defined among CHB patients infected with HIV ($r=0.718$).

We have also set up a positive moderate correlating between qHBsAg in blood serum and the main indicators of cytolysis syndrome - the level of ALT ($r=0.639$) and AST ($r=0.671$) in the blood serum among coinfecting patients, as well as with the liver fibrosis level (according with ARRI test) among CHB patients infected with HIV ($r=0.698$).

There also was defined a negative moderate correlation between qHBsAg in blood serum and CD4+ levels ($r=-0.568$).

Table 1 – qHBsAg correlations with laboratory indicators among CHB patients infected with HIV

Indicator, which is correlating with qHBsAg	Correlation coefficient, r	p	Correlations' strength and directions
HBV DNA, IU/ml	+0,718	$p<0,01$	strong, positive
Fibrosis level	+0,698	$p=0,01$	moderate, positive
AST, U/L	+0,671	$p=0,05$	moderate, positive
ALT, U/L	+0,639	$p<0,01$	moderate, positive
CD4+, cells/ml	-0,568	$p<0,01$	moderate, negative
HIV VL, cop/ml	+0,381	$p=0,003$	mild, positive

There were 1.33 times more people with elevated ALT in the blood serum, 1.92 times more patients with signs of profound liver fibrosis / cirrhosis of the (F3-4) and 1.35 times

more with high HBV DNA level among CHB patients infected with HIV, compared with patients with CHB along before treatment began (tab. 2).

Table 2 – Laboratory and clinical indicators among patients with chronic hepatitis B before TDF prescription

Indicator	CHB/HIV coinfected (n=60), abs. (%)	CHB monoinfected (n=60), abs. (%)	OR [95% CI]	p
«HBeAg negative CHB phase»	37 (61,67%)	27 (45,00%)	1,966 [0,950 – 4,071]	p=0,06
*ALT>40 IU/ml	44 (73,33%)	33 (55,00%)	2,250 [1,046 – 4,838]	p<0,05
AST>40 IU/ml	42 (70,00%)	34 (56,67%)	1,784 [0,841 – 3,785]	p=0,130
*Fibrosis level F3- F4	23 (38,33%)	12 (20,00%)	2,486 [1,096 – 5,641]	p<0,05
*HBV DNA>2000 IU/ml	42 (70,00%)	31 (51,67%)	2,183 [1,032 – 4,617]	p<0,05

Notes: *p<0,05 – significant difference between CHB/HIV coinfecting and CHB monoinfected.

Clinical and laboratory parameters were monitored for more than 12 months of therapy after initiation of antiviral therapy for both coinfecting and monoinfected patients.

According to our data, there is a decrease of the intensity or disappearing of the main clinical manifestations in accordance with the treatment duration under the influence of antiviral therapy among patients with CHB coinfecting with HIV. Thus, the number of patients with manifestations of astheno-vegetative syndrome decreased by 1.92 times after less than 6 months of therapy, in frames “less than 6 months - more than 12 months” by 2.82 times, and after more than 12 months - by 3.20 times (Fig. 1).

Complaints of nausea and loss of appetite after less than 6 months of therapy decreased by 1.68 times, in frames “less than 6 months - more than 12 months” - by 2.47 times, and more than 12 months - by 3.01 times, and complaints of “the liver discomfort” decreased by 1.20, 2.00 and 3.00 times, respectively. Arthralgias and osalgias were found in 3.00 times fewer among CHB patients coinfecting with HIV in the period “more than 12 months after the start of treatment”.

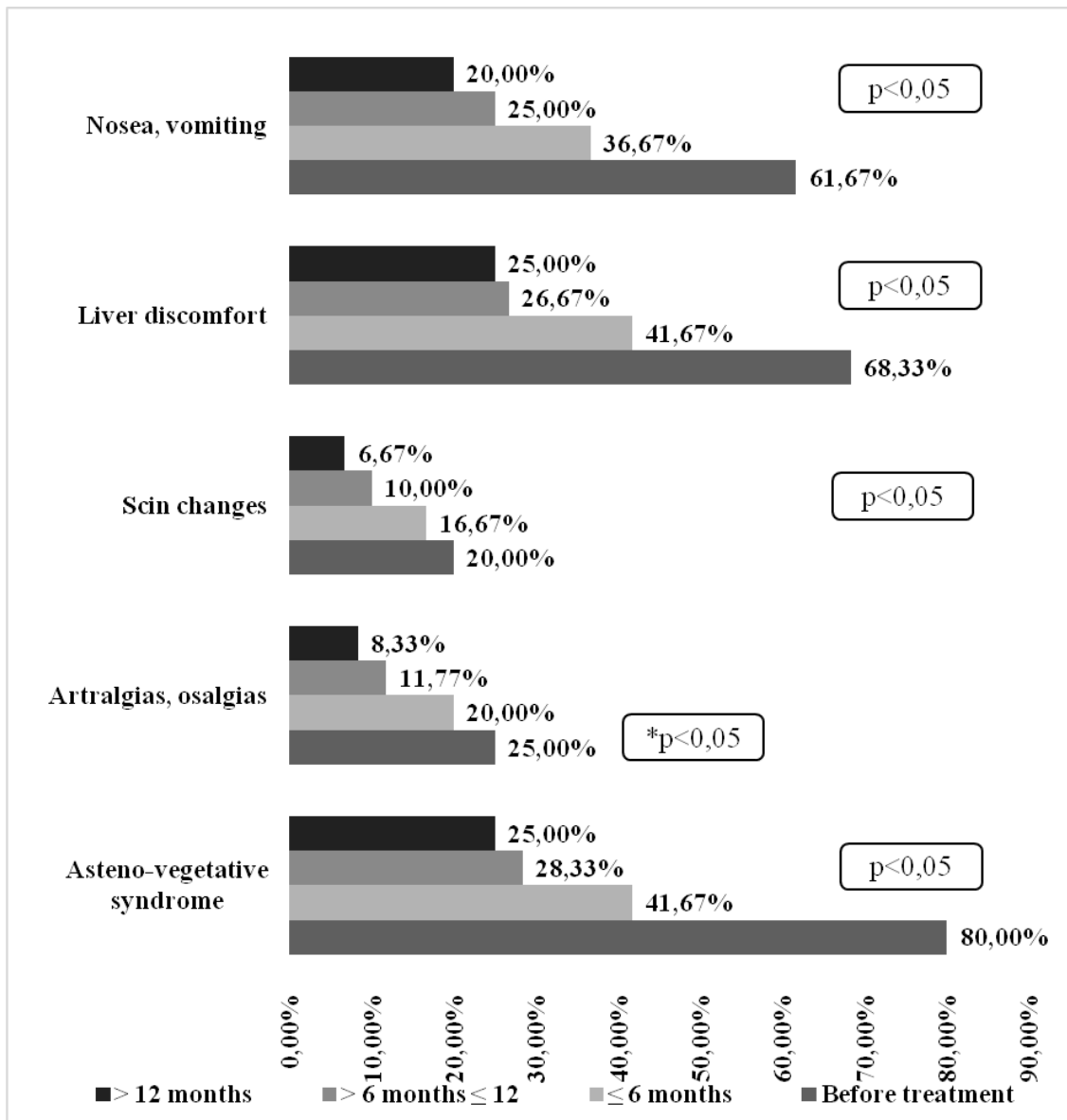


Figure 1 – CHB symptoms among CHB/HIV coinfected patients during consecutive treatment periods.

Notes: *p<0,05 – significant differences concerning “artralgias, osalgias” will appear only between “start of treatment period” and “more than 12 months of treatment period”.

A similar pattern was observed in the treatment of monoinfected CHB patients. The greatest dynamics was recorded in the manifestations of astheno-vegetative syndrome, the number of patients with its symptoms decreased by 2.25 times after “less than 6 months of therapy”, by 3.30 times after “less than 6 months - more than 12 months”, by 4.67 times after “more than 12 months from the treatment beginning” (Fig. 2). The number of patients with complaints of “nausea and loss of appetite” decreased after “more than 12 months of therapy” by 3.08 times, patients “with the liver discomfort” by 2.43 times.

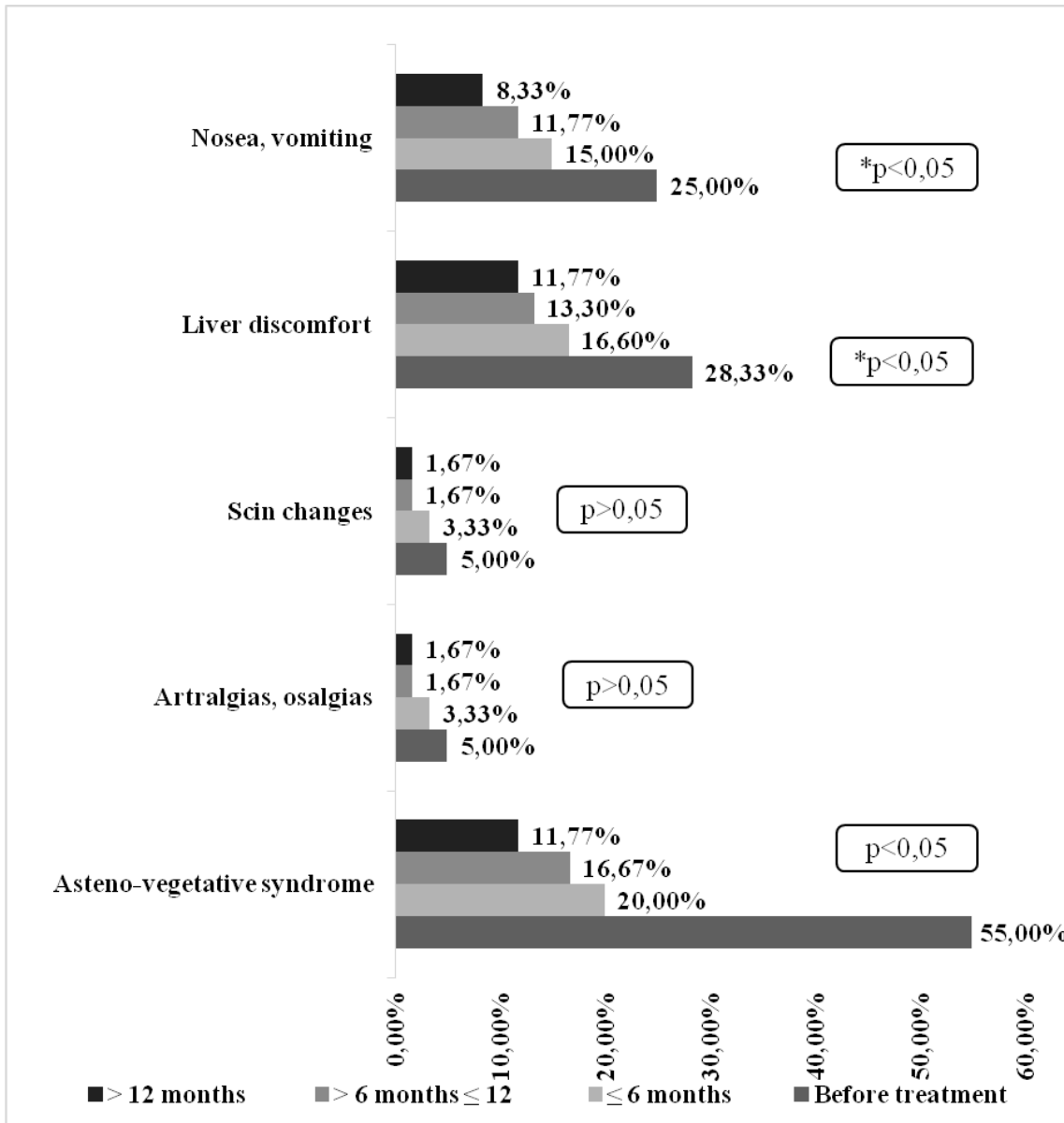


Figure 2 – CHB symptoms among CHB monoinfected patients during consecutive treatment periods.

Notes: *p<0,05 – significant differences concerning “nosea, vomiting” as well as “liver discomfort” will appear only between “start of treatment period” and “more than 12 months of treatment period”.

However, a significant difference in the dynamics of the disease clinical manifestations disappearance after the antiviral therapy starting between groups of patients CHB/HIV coinfecting and CHB monoinfected was not found.

The level of ALT in the serum before treatment was 1.14 times higher among CHB patients coinfecting with HIV infection than in monoinfected CHB patients (Fig. 3). We found that there is a slight increase in serum ALT after “a period ≤ 6 months of antiviral therapy” in 1.10 times among CHB/HIV coinfecting patients, which is followed by a decrease during “a

period of > 6 months ≤ 12 months” and “a period of > 12 months of treatment” in 1.20 and 1.46 times, respectively. There was a decrease in serum ALT levels according to the timing of treatment among monoinfected patients at the same time. Thus, after “a period of ≤ 6 months antiviral therapy” - by 1.14 times, after “a period of > 6 months ≤ 12 months” – by 1.24 times and after “a period of > 12 months of treatment” – by 1.28 times.

We also found a significant difference in serum ALT levels between groups of patients with coinfection and monoinfection at certain stages of treatment. Thus, this indicator was 1.42 times higher among CHB patients coinfecting with HIV after “a period of ≤ 6 months of antiviral therapy” and 1.18 times higher in “a treatment period of > 6 months ≤ 12 months (Fig. 3).

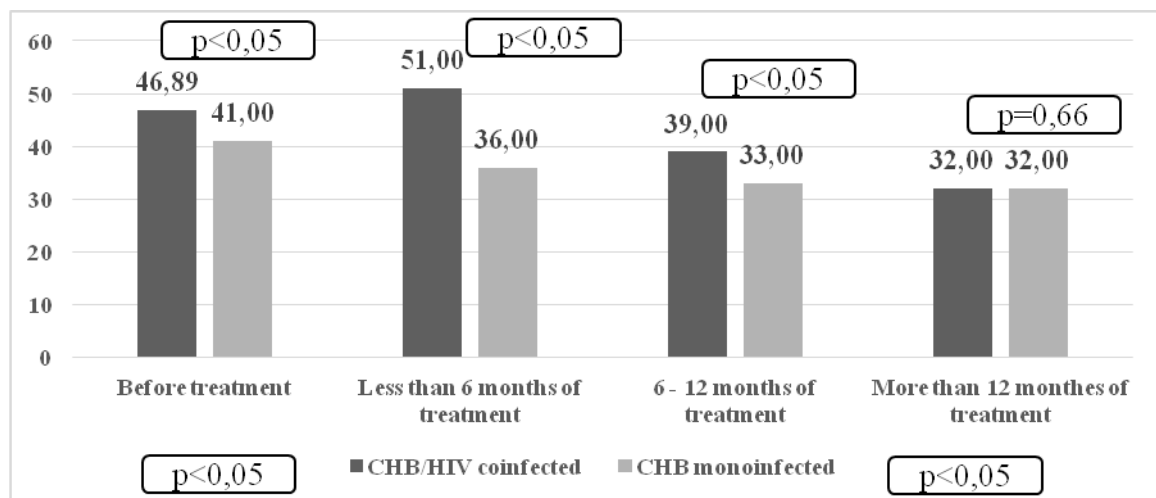


Figure. 3 – ALT levels among patients with chronic hepatitis B during different treatment periods.

Notes: p<0,05 – significant differences between coinfecting and monoinfected groups apart from the period “more than 12 months of treatment” - p=0,66;

p<0,05 – between different treatment period separately among CHB/HIV coinfecting patients as well as among CHB monoinfected patients.

Our analysis revealed a significant decrease in serum qHBsAg among CHB patients coinfecting with HIV as well as with CHB monoinfected, respectively to the treatment duration. Thus, qHBsAg in the serum decreased by 1.56 times after 6 months of therapy, by 6.61 times - within period of 6 - 12 months, and by 21.10 times - after 12 months of treatment among coinfecting patients. A similar pattern occurred among monoinfected patients in whom serum qHBsAg decreased 1.99 times after 6 months, 2.51 times - after 6 to 12 months, and 3.24 times - after 12 months of therapy (Fig. 4).

We also found 4.20 times higher serum qHBsAg among CHB patients coinfecting with HIV infection after 6 months of treatment compared with CHB monoinfected patients. No significant difference in serum qHBsAg was found during further treatment period (Fig. 4).

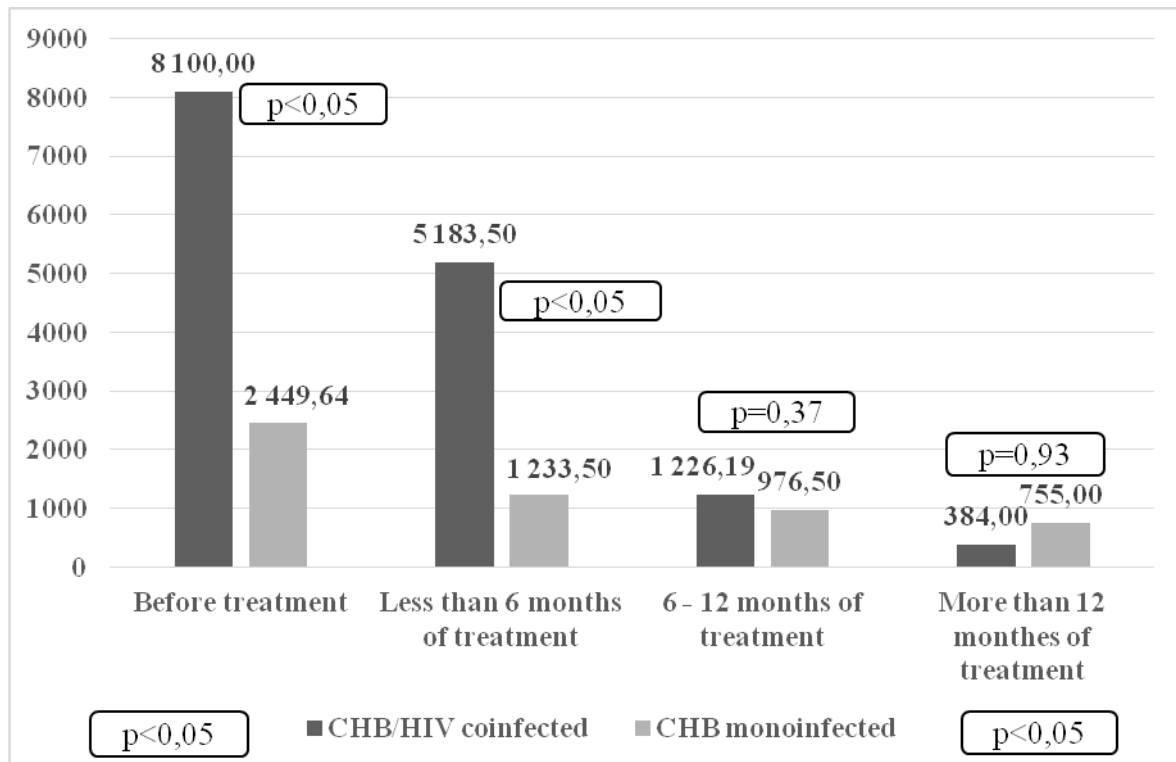


Figure 4 – qHBsAg levels among patients with chronic hepatitis B during different treatment periods.

Notes: p<0,05 – significant differences between coinfecting and monoinfected groups apart from the periods “6 – 12 months of treatment” (p=0,37) “more than 12 months of treatment” (p=0,97);

p<0,05 – between different treatment period separately among CHB/HIV coinfecting patients as well as among CHB monoinfected patients.

We found a significantly higher number of patients who did not experience "ALT flare", both among coinfecting as well as among monoinfected patients. Thus, there were 1.86 times more such individuals among CHB patients coinfecting with HIV, and 4.00 times more among patients with CHB monoinfection. (Fig. 5). No differences were found between patients with ALT flare between groups.

A comparative analysis of the qHBsAg dynamics in the serum of CHB patients coinfecting with HIV depending on the level of ALT in the serum at different stages of treatment found that qHBsAg in the serum of patients with ALT flare » was 5.13 times higher in comparison with patients without a significant increase in serum ALT only in “the treatment period of ≤ 6 months” (Tab. 3). There was no significant difference in the

subsequent stages of therapy. It has been also found the qHBsAg decrease in serum according to the duration of treatment in each group of patients. HBsAg levels decreasing occurred 1.31, 14.48 and 72.72 times during consecutive periods “after ≤ 6 months”, “ > 6 months ≤ 12 months” and “ >12 months” among patients with ALT flare, respectively.

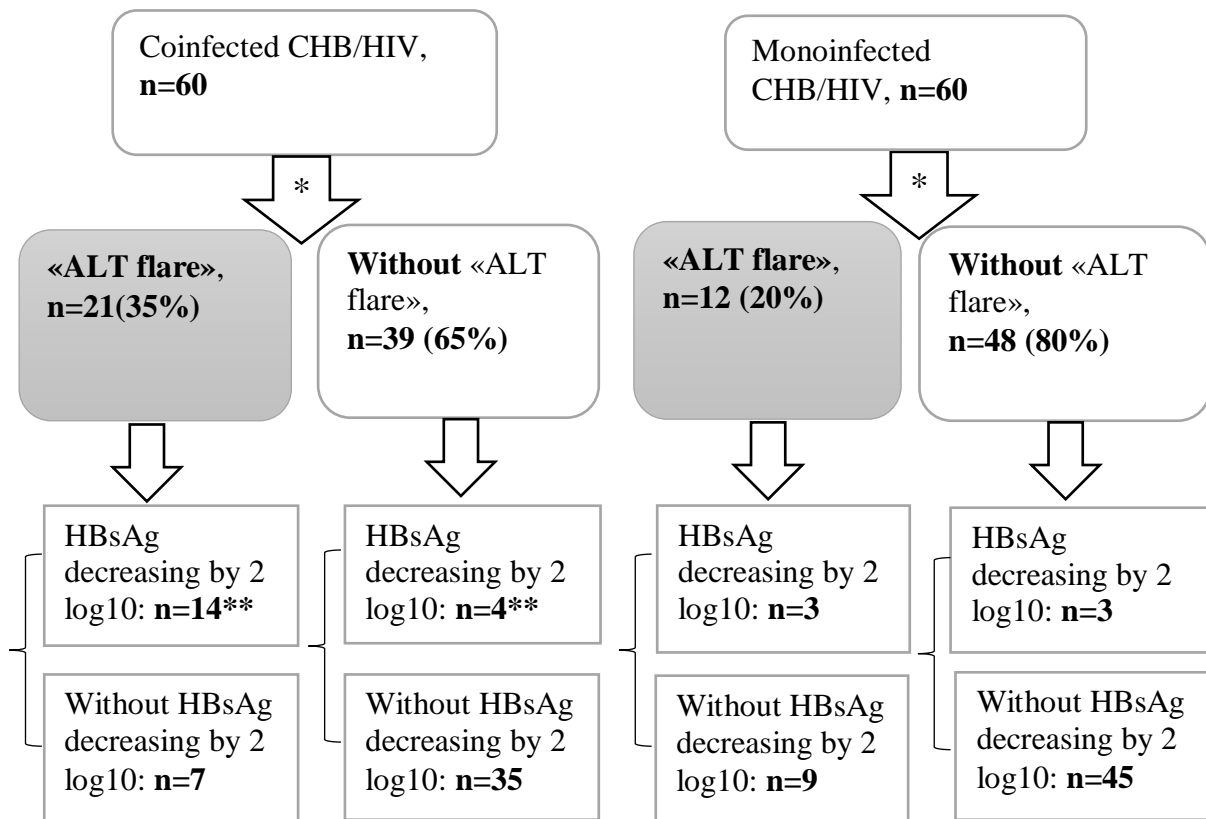


Figure 5 – «ALT flare» influence on further HBsAg decreasing by 2 log10 in course of antiviral therapy.

Notes: * $p < 0,05$ – between «ALT flare» and «Without «ALT flare»» among coinfected patients (between $n=21$ and $n=39$);

* $p < 0,05$ – between «ALT flare» and «Without «ALT flare»» among monoinfected patients (between $n=12$ and $n=48$);

** $p < 0,05$ – among CHB/HIV coinfected patients with «ALT flare», who experienced HBsAg decreasing by 2 log10 ($n=14$ from 21) and CHB monoinfected patients «Without «ALT flare»» who experienced HBsAg decreasing by 2 log10 ($n=4$ from 39).

There was a slightly smaller decrease in serum qHBsAg in patients without a significant increase in serum ALT - by 1.39, 2.62 and 4.41 times respectively.

We calculated the qHBsAg dynamics in the serum of a group of CHB patients coinfected with HIV, depending from the initial amount of CD4 + count. Thus, the greatest decrease in serum qHBsAg was observed in patients with an initial amount of CD4 + < 350

cells / μl . HBsAg levels in serum of this subgroup decreased already in “the treatment period of ≤ 6 months” by 1.63 times, in “the period of > 6 months ≤ 12 months” - by 13.84 times, and in “the period of > 12 months” - by 42.00 times (Tab. 4).

Table 3 - HBsAg levels in the serum of patients with CHB depending from “ALT flare” at the different treatment periods

Treatment periods	CHB/HIV coinfectd with «ALT flare», n=21*	CHB/HIV coinfectd without «ALT flare», n=39**	p ₁₋₂
	1	2	
	qHBsAg, IU/ml, Mediana (Q1 – Q3)		
Before treatment	15925,45 (9788,81 – 48485,89)	3282,21 (775,00 – 15543,67)	p<0,05
≤ 6 months	12100,00 (6515,84 – 27241,34)	2357,44 (208,88 – 6675,02)	p<0,05
> 6 months ≤ 12 months	1100,00 (487,25 – 8606,25)	1250,00 (35,62 – 5800,00)	p=0,209
> 12 months	219,00 (78,50 – 5266,50)	745,00 (21,00 – 2983,00)	p=0,653

Notes: Each group comparison at the different treatment periods:

*p<0,05 – among CHB/HIV coinfectd with «ALT flare»;

**p<0,05 – among CHB/HIV coinfectd without «ALT flare».

Table 4 - HBsAg levels in the serum of CHB/HIV coinfectd patients depending from CD4 + count at the different treatment periods

Treatment periods	Subgroup «baseline CD4+ count <350 cells/ μl », n=26	Subgroup «baseline CD4+ count 350 – 500 cells/ μl », n=20	Subgroup «baseline CD4+ count >500 cells/ μl », n=14	p ¹⁻³
	1	2	3	
	qHBsAg, IU/ml, Me (Q1 – Q3)			
Before treatment	19050,17 (8526,25 – 47742,94)	4945,50 (2061,41 – 20087,83)	525,00 (284,50 – 5692,53)	p ¹⁻³ <0,05
≤ 6 months	11675,00 (5592,52 – 35468,17)	3227,96 (973,38 – 7330,65)	192,24 (73,64 – 4875,00)	p ¹⁻³ <0,05
> 6 months ≤ 12 months	1375,00 (633,27 – 9783,93)	2525,12 (582,36 – 5825,20)	36,71 (7,54 – 3340,00)	p ¹⁻³ <0,05
> 12 months	453,50 (97,00 – 6302,75)	932,50 (151,25 – 4373,00)	27,00 (1,51 – 1538,25)	p ¹⁻³ <0,05
p ¹ , p ² , p ³	p ¹ <0,05	p ² <0,05	p ³ <0,05	N/A

Notes: p<0,05 – significant differences

Serum HBsAg levels in case of initial CD4 + count > 500 cells / μ l decreased under the influence of treatment by 2.23 times in “the treatment period of ≤ 6 months”, 14.30 times within “the period of > 6 months ≤ 12 months” and the greatest decrease was recorded in “the period of > 12 months” – by 19.44 times.

The lowest serum qHBsAg dynamics across treatment periods was discovered in the group of CHB patients coinfecting with HIV with an initial amount of CD4 + count 350 - 500 cells / μ l. The decrease in serum qHBsAg occurred by 1.53, 1.95 and 5.30 times after ≤ 6 months, > 6 months ≤ 12 months and > 12 months of therapy, respectively.

We also found changes in serum qHBsAg among CHB/HIV coinfecting patients across the treatment periods in accordance with Δ CD4 + (the difference between CD4 + count after first 3 months of HAART and CD4 + count before HAART).

Thus, serum HBsAg level was 2.47 times higher in patients with Δ CD4 + > 100 cells / μ l compared with patients whose Δ CD4 + 0 - 100 cells / μ l (Tab. 5).

Table 5 - HBsAg levels in the serum of CHB/HIV coinfecting patients depending from Δ CD4+ at the different treatment periods

Treatment periods	Subgroup « Δ CD4+ > 100 cells/ μ l», n=14	Subgroup « Δ CD4 0 - 100 cells/ μ l», n=46	p^{1-2}
	1	2	
	qHBsAg, IU/ml, Me (Q1 – Q3)		
Before treatment	13550,00 (9606,00 – 63617,69)	5482,68 (949,16 – 20508,75)	$p^{1-2}=0,004$ ($p<0,05$)
≤ 6 months	11675,00 (6723,80 – 24087,00)	3227,96 (249,31 – 11333,88)	$p^{1-2}=0,003$ ($p<0,05$)
> 6 months ≤ 12 months	764,92 (286,25 - 1200,00)	2690,12 (71,36 – 8982,12)	$p^{1-2}=0,256$
> 12 months	108,00 (73,75 – 222,50)	1214,00 (42,75 – 5787,00)	$p^{1-2}=0,028$ ($p<0,05$)
p^1, p^2	$p^1<0,05$	$p^2<0,05$	N/A

Notes: $p<0,05$ – significant differences.

The serum qHBsAg in “a treatment period of ≤ 6 months” decreased by 1.16 times among subgroup of CHB/HIV coinfecting patients with « Δ CD4+ > 100 cells/ μ l » and was 3.62 times higher than in the subgroup of CHB/HIV coinfecting patients with Δ CD4 + 0 - 100 cells / μ l during the same period. The serum qHBsAg in “a treatment period of > 6 months ≤ 12 months” decreased by 17.71 times among subgroup of CHB/HIV coinfecting patients with « Δ CD4+ > 100 cells/ μ l » and was 3.52 times lower than in the subgroup of CHB/HIV

coinfected patients with $\Delta CD4 + 0 - 100$ cells / μl during the same period. The serum qHBsAg “after > 12 months of therapy” decreased by 125.46 times among subgroup of CHB/HIV coinfected patients with « $\Delta CD4+ > 100$ cells/ μl » and was 11.24 times lower than in the subgroup of CHB/HIV coinfected patients with $\Delta CD4 + 0 - 100$ cells / μl during the same period.

Discussion: The results obtained during the study indicate a significant reduction in all assessed clinical manifestations among CHB/HIV coinfected as well as among CHB monoinfected patients after “period > 12 months from the start of treatment” ($p < 0.05$). However, a significant difference in the dynamics of the reduction of CHB clinical manifestations after antiviral therapy starting between groups of patients were not found.

The dynamics of ALT and qHBsAg were assessed during the established treatment periods in order of further the antiviral therapy effectiveness monitor, and qHBsAg was measured depending on the presence of "ALT flare", CD4 + count level and $\Delta CD4 +$.

Thus, obtained results indicate that there was a slight increase by 1.10 times in serum ALT during “a period ≤ 6 months of antiviral therapy”, followed by a decrease by 1.20 times in “frames of > 6 months ≤ 12 months” and by 1.46 times in “a period > 12 months of treatment” among CHB/HIV coinfected patients respectively. We also found a significant difference in serum ALT levels between groups of patients with co- and mono-infection. Specifically, ALT is by 1.42 times higher in patients with CHB/HIV coinfection after “a period of ≤ 6 months of antiviral therapy” and by 1.18 times higher in “a treatment period > 6 months ≤ 12 months” than among monoinfected with CHB.

The ALT levels increase soon after the start of treatment forced us to think about the occurrence of "ALT flare", as mentioned by the literature sources [3, 6, 8, 9, 13]. It is known from the available sources that "ALT flare" usually occurs during first 12 months after antiviral therapy starting, which is usually associated with effective antiviral therapy, in cases when such factors as virological failure and drug-induced liver damage were excluded [3, 4, 6, 16]. A serum HBsAg level decreased by 1.56 times during “a period ≤ 6 months of antiviral therapy”, by 6.61 times in “frames of > 6 months ≤ 12 months”, and by 21.10 times during “a period > 12 months of treatment” among CHB/HIV coinfected patients. A rapid dynamic of qHBsAg after the antiviral therapy starting according with data obtained Yang R. et al. serves as a predictor of further clearance among CHB/HIV coinfected patients [14]. Therefore, it was necessary to find out the reasons for the faster decrease in qHBsAg in coinfected individuals.

Both HIV-positive and HIV-negative patients with “ALT flare” were more likely to achieve a 2 log₁₀ decrease in qHBsAg compared to those who did not experience a

paradoxical ALT increase during the first year after the antiviral therapy starting, as confirmed by the literature data [2, 6, 11, 16]. However, “ALT flare” occurred more often in CHB/HIV coinfecting patients. Our comparative analysis of the serum qHBsAg dynamics of CHB patients coinfecting with HIV depending on the ALT level in the serum at the different treatment periods established, that the serum qHBsAg was by 5.13 times higher only in “the treatment period of ≤ 6 months” among patients with ALT flare comparing with patients without a significant increased serum ALT., There was no significant difference in the subsequent stages of therapy, which indicates a rapid qHBsAg decrease among coinfecting patients with "ALT flare".

A serum qHBsAg decreased under the influence of treatment by 2.23 times after ≤ 6 months, by 14.30 times within > 6 months ≤ 12 months and the greatest decrease was recorded after > 12 months of therapy – by 19.44 times in the case if initial amount of CD4 $+ > 500$ cells / μ l. The lowest dynamics of qHBsAg in serum during treatment was recorded in the group of coinfecting patients with an initial amount of CD4 + 350 - 500 cells / μ l. Decreasing of serum qHBsAg occurred by 1.53, 1.95 and 5.30 times at the same treatment periods of last discussed group. At the same time, the greatest decrease in serum qHBsAg under the influence of treatment by 1.63, 13.84 and 42.00 times, respectively, accordingly with the therapy periods, was observed in patients with an initial CD4 + count < 350 cells / μ l. This fact is probably associated with the occurrence of the “immune recovery inflammatory syndrome” in coinfecting patients. The growth of CD4 + counts after HAART with dual activity starting with tenofovir switched on a mechanism that increases the likelihood of HBsAg clearance among HIV-positive patients [4, 7, 9, 12, 16,].

Δ CD4 + count was used to prove the relationship between the qHBsAg dynamics and the recovery of the immune system among CHB/HIV coinfecting patients. Data were obtained according to which in coinfecting patients with Δ CD4 + > 100 cells / μ l at the beginning of therapy qHBsAg in serum was 2.47 times greater than in patients with Δ CD4 + 0 - 100 cells / μ l. The serum qHBsAg in “a treatment period of ≤ 6 months” decreased by 1.16 times among subgroup of CHB/HIV coinfecting patients with « Δ CD4+ > 100 cells/ μ l » and was 3.62 times higher than in the subgroup of CHB/HIV coinfecting patients with Δ CD4 + 0 - 100 cells / μ l during the same period. The serum qHBsAg in “a treatment period of > 6 months ≤ 12 months” decreased by 17.71 times among subgroup of CHB/HIV coinfecting patients with « Δ CD4+ > 100 cells/ μ l » and was 3.52 times lower than in the subgroup of CHB/HIV coinfecting patients with Δ CD4 + 0 - 100 cells / μ l during the same period. The serum qHBsAg “after > 12 months of therapy” decreased by 125.46 times among subgroup of

CHB/HIV coinfecting patients with « $\Delta CD4+ > 100$ cells/ μ l » and was 11.24 times lower than in the subgroup of CHB/HIV coinfecting patients with $\Delta CD4 + 0 - 100$ cells / μ l during the same period. Obtained data are comparable with the literature, where similar results were described [9, 12, 15, 16].

Conclusions:

1. The manifestations of astheno-vegetative syndrome, complaints of nausea and loss of appetite, liver discomfort decreased by 1.20-3.20 times among CHB/HIV coinfecting patients. Arthralgias and osalgias were found in three times fewer patients number in “a period of > 12 months after the start of treatment”. There was a slight increase by 1.10 times in serum ALT in “a period of ≤ 6 months of antiviral therapy” with a subsequent decrease by 1.20-1.46 times in “a period of > 6 months of therapy”.

2. There was a decrease in the serum qHBsAg of coinfecting patients in accordance with the duration of therapy by 1.56-21.10 times, and in case of the presence of "ALT flare" by 1.31-72.72 times.

3. The greatest decrease in serum qHBsAg by 1.63-42.00 times during HAART was also observed in patients with an initial $CD4 +$ count < 350 cells / μ l. A serum qHBsAg was 11.24 times lower after > 12 months of therapy in the group of CHB/HIV coinfecting patients with $\Delta CD4 + > 100$ cells / μ l compared with the group of patients with $\Delta CD4 + 0 - 100$ cells / μ l.

4. It is necessary to conduct further multifactor analysis to determine those factors which could influence on further HBsAg by 2 log₁₀ and HBsAg clearance.

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